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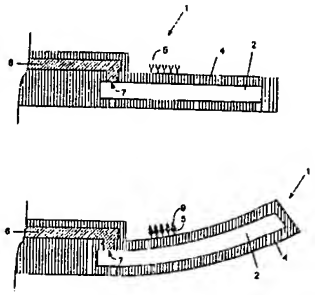
(54) Title: A SENSOR FOR USE IN DETECTION OF A TARGET SUBSTANCE IN A SAMPLE



(57) Abstract: The present invention relates to a micromechanical sensor (1) for detecting a target substante in a liquid or a gas and comprising at least one sensor unit with a capture surface (30) and at least one conducting element (2) of an electrically conducting material with a pair of wires for applying an electrical field over the conducting element. The conducting element comprises at least two divisional units (34) and the conducting element has a larger conductance in one sensor state than in another sensor state due to a change in contact area for electrical conduction between two or more divisional units on deformation from one sensor state to another in response to surface stress arising from a chemical interaction at the capture surface. The conducting element may preferably comprise 2-100 divisional units or even more which divisional units may be systemically arranged or randomly ordered e.g. in a non-conductive dispersant material. In a preferred embodiment, the sensor is used to detect DNA, and the conducting element (2) contains carbon nanowires.

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A sensor for use in detection of a target substance in a sample

Field of invention

The present invention relates to a sensor for use in detection of one or more target substances, such a biological molecule e.g. an antibody or a nucleic acid; a bacteria, a virus, a drug, alcohol or explosives in a sample, such as a fluid sample e.g. gas or liquid.

Description of the background art

Sensors of the above type are well known from the literature. Examples of known sensors includes gas sensors e.g. as described in "smart single-chip gas sensor microsystem" C.Hagleitner et al. Nature 414, November 15th, 2001, 293-296, and EP patent publication No. 72 744; AFM probes as described in "5X5 2D AFM cantilever arrays a first step towards a Terabit storage device, M Lutwyche et al, sensor and Actuators 73 (1999) 89-94.

For stress formation studies in aqueous environments, micrometer-sized cantilevers with optical read-out have been disclosed in the articles Berger, R., Gerber, Ch., Lang, H.P. & Gimzewski, J.K. Micromechanics: A toolbox for femtoscale science: "Towards a laboratory on a tip". *Microelectronic Engineering*. 35, 373-379 (1997), and O'Shea, S.J., Welland, M.E. Atomic force Microscopy stress sensors for studies in liquids. *J. Vac. Sci. Technol. B.* 14, 1383-1385 (1996).

In WO 00/66266 a sensor is described for monitoring the

biochemical properties of fluids in a microfluid handling system. The sensor comprise one or more flexible structures, e.g. cantilevers, who change their mechanical structure, such as surface stress, upon reaction of an analyte in the fluid with a substance provided by a capture layer coated on the flexible structure.

The change in mechanical structure may be interrelated to a change in electrical resistance of a piezoresistive material integrated in the flexible structure. By applying a voltage to the piezoresistive material the change of resistivity or piesoresistive material can be detected.

Cantilever-based sensors with integrated piezoresistive read-out are described by Thaysen, J., Boisen, A., Hansen, O. & Bouwstra, S. AFM probe with piezoresistive read-out and highly symmetrical Whetstone bridge arrangement. *Proceedings of Transducers'99*,1852-1855 (Sendai, 1999). Hereby the stress changes on, the cantilever sensors can be registered directly by the piezoresistor. Moreover, integrated read-out greatly facilitates operation in solutions since the refractive indices of the liquids do not influence the detection. Each sensor has a built-in reference cantilever, which makes it possible to subtract background drift directly in the measurement. The two cantilevers are connected in a Wheatstone bridge, and the stress change on the measurement cantilever is detected as the output voltage from the Wheatstone bridge.

Another type of sensor for detection of target substances uses the unique properties of piezoelectric materials for the detection of the presence of a substance in a fluid.

The discovery of a linear relationship between the change

in the oscillating frequency of a piezoelectric crystal and the mass variation on the crystal as a result of binding or adsorption phenomena allowed the possibilities of using piezoelectric materials as chemical sensors, where the change of mass of the piezoelectric crystal due to adherence or binding of a substance can be detected by a change of frequency of the oscillating crystal.

Such biosensors for determining the presence of an analyte in a liquid are e.g. disclosed in WO 9704314 and WO 9840739. These biosensors comprise a member of a recognition pair immobilized to the surface of a metal plate e.g. one of the electrodes on the piezoelectric sensor unit.

Summary of the invention.

The invention provides a completely new class of sensors for detection of a target substance in a sample, such as a liquid or gas sample. The sensor of the invention thus provides a new alternative to the above described sensors.

The sensor according to the invention has a high sensitivity and is in general simple to produce. The sensor according to the invention has several advantages compared to prior art sensors, as it will be explained further below.

The sensor is defined in the claims and is mainly based on the idea of using change in contact areas between pieces of conducting material as an indication of the presence of a target substance.

The sensor according to the invention thus comprises a sensor unit with a capture surface and a conduct element of conducting material. The shape of the sensor unit

changes due to interaction between the capture surface and the target substance whereby a temperature change, a mass change and/or a change is surface stress of the sensor unit is provided. This mechanical change deforms the conduct element whereby a change of conductance can be registered. It is believed that the change in conductance is due to a change of contact areas between pieces of conducting material also designated "divisional units" of the conduct units.

Disclosure of the invention

The sensor according to the invention comprises at least one sensor unit with a capture surface.

In one embodiment the capture surface is provided by one or a few molecules also designated "binding partners". In the following the term "binding partner" means a molecule or a complex of molecules which is capable of interacting with a target substance. The target substance may preferably be as disclosed in the embodiments below. The interaction means a simple attraction, such as an ionic attraction or a hydrophobic/hydrophilic attraction or a chemical bond such as a hydrogen bond, a ionic bond or a covalent bond. In general it is desired that the interaction is a bond, in particular when the sample comprises non-target substances which are of the same type (e.g. proteins) as the target substance, since the noise level when the chemical interaction is a bond may be kept very low.

In one embodiment the interactions between the total number of binding partners and the target substances are sufficient to provide a stress whereby the sensor unit is deformed from one sensor state to another sensor state.

In one embodiment the capture surface is provided by one or more binding partners, such as up to 10 binding

partners, such as up to 100 binding partners, such as up to 1000 binding partners, such as up to 10000 binding partners, such as up to 10^{12}. The capture surface may thus be provided by one single or a few molecule layers comprising one or more binding partners.

In one embodiment the capture surface comprises a plurality of binding partners. The capture surface may e.g. be provided essentially by a plurality of binding partners.

In one embodiment the sensor according to the invention is provided by a layer containing binding partners. This layer is designated a "capture layer". The capture layer may e.g. comprise up to several million of binding partners such as up to 10 binding partners, such as up to 100 binding partners, such as up to 1000 binding partners, such as up to 10000 binding partners, such as up to 10^{12}. The capture layer may also comprise other molecules. These molecules may e.g. be inert to the interaction between the target substance and the binding partner. In one embodiment the other molecules in the capture layer is capable of amplifying the surface stress provided when a target substance interacts with a binding partner. This amplifying could e.g. be provided due to sterically influences of the other molecules.

In one embodiment the capture surface is provided by a capture layer comprising one or more of the materials selected from the group consisting of metals, such as Au, Ag and Pt and polymeric materials, such as polymeric materials selected from the group consisting of thermoplastics such as thermoplastic elastomers including block copolymer such as SEBS, SBS, SIS, TPE-polyether-amide, TPE-polyether-ester, TPE-urethanes, TPE PP/NBR, TPE-PP/EPDM, TPE-vulcanisates and TPE-PP/IIR; rubbers such as butadiene rubber, isoprene rubber, silicon rubber, nitrile rubber, styrene-butadiene rubber and

urethane rubber; acrylates; polyolefins such as polyethylene, polypropylene and polybutylene including its isomers; polyesters; polystyrene; polyacrylates; polyethers; and polyurethane. The binding partners may e.g. be embedded or linked to one or more of these materials.

In one embodiment the capture surface is provided by a capture layer comprising a coating of a material selected from the group consisting of oxides, sulphides and selenides. The one or more binding partner may be linked to this layer.

The binding partners may in principle be of any kind as it is generally known from the art e.g. as disclosed in WO 99/38007, WO 02/48701, US 6,289,717 and WO 0066266 which, with respect to disclosure concerning binding partners are hereby incorporated by reference.

In one embodiment the capture surface comprises one or more binding partners in the form of one or more binding components. The binding components preferably comprise one or more of the components selected from the group of explosives, alcohols, drugs, enzymes and one or more biomolecules, such as one or more biomolecules in the form of tissue, cells, body fluids, blood components, microorganism, derivatives thereof, or parts thereof.

The term one or more biomolecules includes one or more biomolecules of microbial, plant, animal, viral, fungal, or human origin or synthetic molecules resembling them, preferably selected from the group consisting of proteins, glyco proteins, nucleic acids, such as RNA, DNA including cDNA, PNA, LNA, oligonucleotides, peptides, hormones, antigens, antibodies, lipids, sugars, carbohydrates, and complexes including one or more of these molecules, said biomolecule or molecules preferably being selected from the group consisting of nucleic

acids, antibodies, proteins, protein complexes and enzymes,.

In one embodiment the capture surface comprises one or more binding partners in the form of molecules comprising a functional group selected from the group consisting of -OH, -CHO, -COOH, -SO3H, -CN, -NH2, -SH, -COSH, COOR, halide.

The one or more binding partners may e.g. be non-specific, however in some applications of the sensor of the invention it is desired that the binding partner is specific for the target substance or target substances.

In one embodiment wherein the capture surface comprises one or more binding partners which are specific, it is thus preferred that the one or more specific binding partners are specific for a target component which may be as the binding component as defined above, e.g. one or more molecules of microbial, viral, plant, animal or human origin or synthetic molecules resembling them, explosives, drugs and alcohols. The target component may preferably be selected from the group consisting of bacterium, virus, fungus, proteins, glyco proteins, nucleic acids, such as RNA, DNA including cDNA, PNA, LNA, oligonucleotides, peptides, hormones, antigens, antibodies, lipids, sugars, carbohydrates, and complexes including one or more of these molecules, said biomolecule or molecules preferably being selected from the group consisting of nucleic acids, antibodies, proteins and protein complexes, enzymes, drugs and receptors.

The binding partner or partners may be linked optionally via a linking molecule to the sensor unit using conventional technology e.g. as disclosed in WO 00/36419, WO 01/04129, WO 96/31557, WO 99/38007, WO 02/48701, US 6,289,717 and WO 0066266, which with reapect to the

linking technology disclosed therein are hereby incorporated by reference.

The sensor unit (or units) of the sensor according to the invention comprises at least one conduct element of an electrically conducting material. The sensor unit is capable of being in at least two sensor states, and it can be deformed from one sensor state to another, wherein the conduct element has a larger conductance in one sensor state than in another sensor state. Thus for each sensor state it is preferred that the conduct element has a different conductance than in the other of the sensor states of the sensor unit. Due to an interaction between a target substance and a binding partner the sensor unit can thus be deformed from one sensor state to another whereby a change of conductance of the conduct element can be detected. In order to detect this change a pair of wires capable of applying an electrical field is applied over the conduct element.

The term conductance may be measured as current/voltage, and accordingly the change may be measured as a change of the other electrical parameters such as a change of current or a change of voltage while preferably keeping one of the parameters of Ohms law constant. The voltage may be direct (direct current DC) or alternating (alternating current AC).

In one embodiment the sensor unit is capable of being deformed from one sensor state to another due to a surface stress or change of surface stress generated on the surface of the sensor unit. In this embodiment the surface stress may be generated due to an interaction between the capture surface and the target substance or substances. This principle of generating surface stress due to chemical interaction on a surface is e.g. known from WO 0066266 and US 6,289,717.

The sensor unit should e.g. be deformable due to a surface stress of less than 10^{-4} N/m, such as less than 10^{-5} N/m, more preferably less than 10^{-4} N/m, more preferably less than 10^{-3} N/m or even more preferably less than 10^{-2} N/m. The smaller the surface stress necessary for deforming the sensor unit from one sensor state to another sensor state, the more sensitive is the sensor unit. In one embodiment the sensor unit has a sensitivity which is sufficient to detect the interaction between an antibody and an antigen.

In one embodiment the change of surface stress is due to a physical interaction at the capture surface e.g. an increase of mass adhered to or bonded to the capture surface.

In one embodiment the change of surface stress is due to a temperature change in the capture surface, e.g. provided by a chemical reaction.

The sensitivity of the sensor with a sensor unit as described above is in general relatively high compared to prior art sensors, since in general the forces necessary to deform the sensor unit from one state to another can be optimised for the desired application.

In one embodiment the sensor unit is capable of being deformed from one state to another due to a deformation force of less than 10^{-10} N, such as between 10^{-9}-10^{-7} N, such as between 10^{-7}-10^{-5} N, or such as between 10^{-5}-10^{-3} N. The desired sensitivity depends largely on the application of the sensor. In situation where the presence of one or a few target molecules should be detected, the sensitivity should be relatively high, whereas in situations where concentrations of a target substance in a fluid should be detected, the sensitivity may be lower, so that the deformation from one state to another sensor state can be provided at the desired level

of stress.

The deformation force is defined as the resulting force applied to the sensor unit. If a force is applied in several directions the deformation force is the sum of the forces, and the direction of the deformation force is the direction of the sum of the forces. The deformation force may in principle have any direction, as long at the deformation force is capable of deforming the sensor unit from one sensor state to another. The direction of the deformation force depends on the placement of the capture surface or surfaces, and optionally fastenings of the sensor unit. If the sensor unit thus is fastened or integrated with a support element, this support element may have influence of the direction of the deformation force.

In one embodiment wherein the sensor unit is essentially sheet-formed with a first and a second major surface e.g. as a cantilever, a diaphragm, a bridge or simply as a sheet, it is desired that the deformation force for deforming the sensor unit from one sensor state to another e.g. in operation is applied against one of the major surfaces. The deformation force may e.g. be applied against one of the major surfaces in a direction perpendicular +- 45 ° to one of the major surfaces, such as in a direction perpendicular +- 15 ° to one of the major surfaces.

In one embodiment wherein the sensor unit is essentially sheet-formed with a first and a second major surface e.g. as a cantilever, a diaphragm, a bridge or simply as a sheet, it is desired that the deformation force for deforming the sensor unit from one sensor state to another e.g. in operation for deforming the sensor unit from one sensor state to another e.g. the deformation force being applied in a direction substantially parallel to one or both of the major surfaces of the sensor unit.

The conduct element may in principle be of any conductive materials, e.g. materials having a specific resistivity such as less than 10^{-1}, such as less than 10^{-2}, such less than 10^{-3}, such as less than 10^{-4}, such as less than 10^{-5}, such as less than 10^{-6}, such as less than 10^{-7} ohm-meters.

The conduct element may e.g. be of one or more materials selected from the group consisting of amorphous polysilicon (single crystal Si), metal or metal containing composition e.g. gold, AlN, Ag, Cu, Pt and Al, conducting polymers such as, doped octafunctional epoxidized novalac e.g. doped SU-8, doped benzocyclobutene e.g. doped BCB, doped polyimide, semi-conductors, doped polymer by ion implantation and composite materials with an electrically non-conducting matrix (a disperse material as disclosed above) and a conducting filler, wherein the filler preferably is selected from the group consisting of amorphous polysilicon (single crystal Si), metal or metal containing composition e.g. gold, AlN, Ag, Cu, Pt and Al, semi-conductors, carbon black, carbon fibres, particulate carbon, carbon nanowires, silicon nanowires.

In one embodiment the conduct element comprises at least two divisional units, and the change in conductance of the conduct element when it is deformed from one sensor state to another is provided by a change in contact area for electrical conduction between two or more divisional units.

The number of divisional units may in one embodiment be 2-100 divisional units, such as 2-20 divisional units, such as 2-10 divisional units, such as 2-5 divisional units.

In an embodiment wherein the divisional units is

dispersed in a disperse material with less conductivity than the material of the conduct element e.g. a non conductive disperse material, the number of divisional unit may be above 100 such as above 1000, such as above 10000. In this embodiment the concentration of the divisional units in the disperse material may e.g. be between 0.1 and 90 vol. %, such as between 1 and 75 vol. %, such as between 5 and 50 vol. %, such as between 10 and 20 vol. %.

The divisional units may in principle have any shape, such as rod-shaped, slab-shaped, ball-shaped and fibre-shaped.

The divisional units may in one embodiment be placed in a chain-like order, or as several chains of conduct elements e.g. in the form of a conducting wire with intermediate cut totally or partly through the wire to thereby provide the divisional units. Other configurations of the divisional units will be described in the following.

In one embodiment the divisional units or at least two divisional units is in one sensor state totally separated from each other. Thereby the conductance in this sensor state where the divisional units is totally separated will be zero. This embodiment is in general very sensitive as the change of conductance through the conduct element will be an on/off configuration i.e. either there is no conductance in one sensor state and there will be conductance in one or several other sensor states, where the conductance is optionally in the other sensor states if there are two or more e.g. can be different from each other.

In one embodiment the divisional units are partly

separated from each other e.g. in the form of a plate or wire of conducting material which comprises one or more trenches extending partly through the material. The trenches, if two or more may have different depth and/or in one or more of the trenches, parts of the material from the conductive element may be removed, so that the needed deformation force for bringing the respective walls of the trenches, also designated the contact areas for electrical conduction of the divisional units together differs from the contact areas for electrical conduction provided by one trench to the contact areas for electrical conduction provided by another trench.

In one embodiment the divisional units are partly separated from each other in the form divisional units applied onto a substrate e.g. a substrate in the form of a insulating layer, in two or more step; one step where a plate or wire of conducting material is applied, and one step where a where divided part of divisional units is formed in the plate or wire using a mask to thereby provide a plate or wire like conduct element with one or more crossing trenches along the length of the wire or plate. The trenches, if two or more may have different depth, so that the needed deformation force for bringing the respective contact areas (trench walls) together for electrical conduction of the divisional units, differs from trench to trench i.e. one force is needed for establishing contact between the contact areas for electrical conduction provided by one trench and another force is needed for establishing contact between the contact areas for electrical conduction provided by another trench.

In one embodiment the conductance of the conduct element is at least 10^{-7} S, such as at least 10^{-6} S, such as at least 10^{-5} S, such as at least 10^{-4} S, such as at least

10^{-3} S, in one sensor state when applying a voltage of up to about 0.1 V. Since the noise of the conduct element in dependence on the type of material used may be e.g. up to about 10^{-4} S, it is often desired to couple the sensor unit to a reference sensor units.

In one embodiment it is desired that the conductance of the conduct element is less than 10^{-8} S, preferably zero S in at least one sensor state.

The conductance in one sensor state of the conduct element relative to the conductance in another sensor state, can in principle be as small as it is possible to detect. When using a sensor with sensor units of micrometer dimensions i.e. having dimensions up to about 500 µm the applied voltage should be kept relatively low e.g. up to about 2 V. When using sensors with larger sensor units e.g. with dimensions length, width, depth, and or diameter of between 0,5 mm to 1 cm, such as between 1 mm and 5 mm the voltage applied may be larger. Care should be taken that the temperature of the conduct element does not increase to a level where the capture layer and/or the target substance is destroyed or changed in a undesired manner e.g. undesired denaturation.

In one embodiment the conductance of the conduct element in one sensor state is at least 2 times, such as at least 3 times, such as at least 5 times the conductance in another sensor state.

In order to have a high sensitivity it is desired in one embodiment that the sensor comprises at least two sensor units, at least one of said sensor units being a reference units. The reference unit may preferably comprise a capture surface with a surface chemistry e.g. in the form of a binding partner which is different from the sensor unit for which the reference unit acts as

reference, preferably said target surface area has been functionalised by linking, preferably by covalently linking of one or more binding partners, wherein said one or more binding partners linked to the surface area of said reference unit or its concentration are different from the sensor unit for which the reference unit acts as reference. Further information relating to this aspect can be found in H. Jensenius et al, 'A microcantilever-based alcohol vapour sensor-application and response model' Appl. Phys. Lett, 76(18) pp. 2615-2617, WO 0066266 and DK patent application PA 2001 01724 which with respect to this aspect including reference units are hereby incorporated by reference.

The reference sensor unit and the sensor unit for which the reference sensor act as a reference may preferably be coupled via a Wheatstone bridge e.g. as described in WO 0066266.

As described above the conductance of the conduct element may change due to a change in surface stress. The conductance of the conduct element may therefore be a function of the surface stress of the sensor unit.

In dependence on the shape of the conduct element including the number of divisional units and their relation to each other and the capture surface or surfaces including the amount and type of binding partners contained on the capture surface, this stress-conductance function may have different shapes.

In one embodiment the function is a declining function when the surface stress of the sensor unit is decreased.

In one embodiment the function is an increasing function when the surface stress of the sensor unit is decreased.

In one embodiment the function is a stepwise function. The stepwise function may e.g. have a number of steps equal to or less than the number of divisional units minus one. In general it is desired in this embodiment that the number of steps may be up to about 25, preferably less than 15, e.g. about 2, 3, 4 or 5 since to many steps may result in a too small sensitivity for the specific steps relative to each other.

The height of the steps may be equal to each other or they may vary.

In one embodiment all contact areas for electrical conduction between divisional units increase in one transition between a first sensor state and a second sensor state. Thereby a one step function is provided.

In one embodiment one contact area for electrical conduction between divisional units increases in one transition between a first sensor state and a second sensor state. In his embodiment the function may comprise several steps.

In one embodiment the function is a continuous function. Such continuous function can e.g. be provided when the conduct element is in the form of divisional units dispersed in a non-, or less-conductive material or where the contact areas between neighbouring divisional units increases continuously due to a deformation force.

The continuous function may e.g. comprise one or more turning points, defined as peak points (high or low) of δS, when the increase of stress is kept constant.

In one embodiment the continuous function comprises a number of equilibrium points less than or equal to the number of divisional units minus one. In practice the

number of equal points should be kept below 25 for one conduct element, such as less than 15, e.g. about 2, 3, 4 or 5 since to many turning points may result in a too small sensitivity for the specific steps relative to each other.

In one embodiment the conduct element is encapsulated in a non-conductive material for thereby preventing short circuiting when the sample to be contacted at the capture surface is a liquid. In general it is not necessary to encapsulate the total of the sensor unit, in one embodiment only the parts that is adapted to come into contact with the liquid is coated with a non-conductive material.

The terms "conductive" and non-conductive" relates to the electrical conductivity unless other is specified.

Generally it is relatively simple to encapsulate the conduct-element with a non-conductive material, and since very deformable materials may be used, a non-conductive material does not necessarily result in a detectable or essentially reduced sensitivity. In some embodiment the non-conductive material do reduce the sensitivity but not to an undesired or unacceptable level.

In one embodiment the shield is of a non-conducting material selected from the group consisting of nitrides, such as silicon nitride and tantalum nitride, non-conducting polymers, epoxies, metal oxides, such as aluminium oxide, silicon oxide, ceramics, diamond films, silicon carbide, tantalum oxide, silicon, glass, mixtures, and combinations thereof.

Examples of useful polymers for the non-conductive material include octafunctional epoxidized novalac e.g.

SU-8, benzocyclobutnene e.g. BCB, polyimide, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacryloni trile, polymethylmetacrylate, polytetrafluoroethylene, polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, bytyl rubber, styrene butadiene rubber and silicon rubber.

In order to have optimal processability, the non-conductive polymer should preferably be of or comprise a material which can act as a photo resistor. Preferred materials include an epoxy resin, preferably selected from the group consisting of epoxy functional resin having at least two epoxy groups, preferably an octafunctional epoxidized novalac. Particularly preferred materials are the non-conductive materials described in US 4882245, which are hereby incorporated by reference. The most preferred material is the octafunctional epoxidized novalac which is commercially available from Celanese Resins, Shell Chemical, MicroChem Inc under the trade name SU-8, and from Softec Microsystems under the trade name SM10#0.

The layer of the non-conductive material may in principle have any thicknesses provided that the sensor is still capable of being deformed from one sensor state to another. The term "deformation" includes any type of deformation that may result in a change of the conductance of the conduct element i.e. bending in one or more directions, twisting, compression and elongation.

As the deformation largely depends on the shape of the sensor unit and the placement and area of the capture surface, the type of bending may be controlled by these features. Further information concerning applicable

deformations can be found e.g. in WO 0066266 and PA 2002 00195 DK. As mentioned above the placement and optionally fixing of the sensor unit e.g. to a support element may also influence the deformation of the sensor unit.

In one embodiment the non-conductive material forms on the conduct element a layer of a thickness of at least 0.1 times the thickness of the conduct element, preferably 0.5 times the thickness of the conduct element, more preferably 1 time the thickness of the conduct element, even more preferably 2 times the thickness of the conduct element.

In one embodiment where the non-conductive material forms a layer on the conduct element, and where the conduct element comprises two major surfaces, the layer of non-conductive material differs in thickness, e.g. so that the layer of non-conductive material onto one of the major surfaces has a first thickness and the layer of non-conductive material onto the other one of the major surfaces has a second thickness. The "major surfaces of the conduct element" means the major surfaces when the divisional units are in maximal contact with each other unless other is specified.

In one embodiment where the non-conductive material is applied to two major surfaces of the conduct element, one of said major surfaces comprising an additional layer of a non-conductive or conductive materials e.g. selected from the group consisting of silicon nitride, silicon oxide, metal oxides, polymers, such as photo-sensitive polymers, octafunctional epoxidized novalac e.g. SU-8, benzocyclobutnene e.g. BCB, polyimide, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacrylonitrile, polymethylmetacrylate, polytetrafluoroethylene,

polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, bytyl rubber, styrene butadiene rubber and silicon rubber. As mentioned this additional layer may e.g. be conductive e.g. in the form material of the above type which has further been doped with conductive elements.

In one embodiment the conduct element comprises 3 or more divisional units, such as up to 50 divisional units, such as between 3 and 25 divisional units, such as between 5 and 10 divisional units. In this embodiment it is desired that the divisional units comprises one contact area for electrical conduction to one or more of the divisional units in one sensor state and no contact area or another contact area for electrical conduction to one or more of the divisional units in another one of the sensor states.

In one embodiment where the capture surface comprises two or more different binding partners, the respective types of binding partners is associated with respective pairs of divisional units which means that that interaction between a target substance for a first type of binding partner and the first type of binding partner results in an increased contact area for electrical conduction the pair(s) of divisional units which is associated with the first binding partner, and interaction between a target substance for a second type of binding partner and the second type of binding partner results in an increased contact area for electrical conduction between the pair(s) of divisional units associated with the second binding partner. In this embodiment it is desired but not essential that the contact area for electrical conduction between the pair(s) of divisional units associated with the first binding partner is preferably not increased due to interaction between a target substance for a second type of binding partner and the second type of binding partner.

The above embodiment may e.g. be provided by placing the binding partners on the capture relative to the divisional units so that the stress provided when interaction with the respective binding partners occur result in a deformation force acting on the respective divisional units.

In one embodiment wherein the binding partner(s) associated with a pair of divisional units is placed relative to the associated pair of divisional units so that a surface stress generated due to interaction with said binding partner(s) results in a force that acts on the associated pair of divisional units to thereby increase the contact area for electrical conduction between said pairs of divisional units it is desired that the binding partner is placed on the surface of a non-conductive layer, placed onto one or both of said associated pair of divisional units.

The first and second binding partner may in one embodiment be specific for the same target substance.

In one embodiment where the sensor unit is sheet formed which include a cantilever shape a bridge shape, a diaphragm shape or simply a sheet, the sheet formed sensor unit comprise two separated capture surfaces which surfaces comprises two different binding partners for different target substance. The conduct element comprise at least 3 divisional units and the sensor unit is capable of being in at least 3 different sensor states wherein none of them results in a completely separation of the divisional units and thereby of a state of non conductance.

In one embodiment wherein the contact areas of two neighbouring divisional units which are capable of coming into contact for electrical conduction in one of the

sensor states are partly or totally separated from each other to a maximal distance in one sensor state. This state of maximal distance is designated "the max separated sensor state for the two neighbouring divisional units". The space between the contact areas of the two neighbouring divisional units in their the max separated sensor state is defined as "the divisional unit spacing for the two neighbouring divisional units". The divisional unit spacing for the two neighbouring divisional units has a thickness defined as the distance between the contact areas of the two neighbouring divisional units. The thickness of the divisional unit spacing for two neighbouring divisional units thus defines the distance between the contact areas for electrical conduction between neighbouring divisional units.

The thickness of the divisional unit spacing for two neighbouring divisional units in their max separated sensor state may e.g. be between 0.1 nm and 100 μm. In one embodiment the thickness of the divisional unit spacing for two neighbouring divisional units in their max separated sensor state is up to about the thickness or up to the width of the one of the two neighbouring divisional units with the smallest of these respective dimensions, wherein the thickness and width is measured in the planes perpendicular to the thickness direction of the divisional unit spacing for the two neighbouring divisional units.

In one embodiment the thickness of the divisional unit spacing for two neighbouring divisional units in their max separated sensor state is up to 1000 nm, such as up to 100 nm, such as up to 10 nm, such as up to 5 nm.

In one embodiment the thickness of the divisional unit spacing for pair wise neighbouring divisional units have a thickness in their respective max separated sensor

states which is up to 1000 nm, such as up to 100 nm, such as up to 10 nm, such as up to 5 nm.

The thickness of one or more of the divisional unit spacings for pair wise neighbouring divisional units may vary or they may be equal to each other. In situations where the divisional units are completely separated it is in most embodiments desired that the distance between the divisional units is substantially equal to each other.

In one embodiment wherein the divisional unit spacings for pair wise neighbouring divisional units have median planes perpendicular to the thickness direction, 2 or more of the divisional unit spacings for pair wise neighbouring divisional units have median planes which are substantially parallel to each other. The median plane is a plane that is essentially parallel to the contact areas for the neighbouring pair of divisional units. In one embodiment it is desired that this median plane is essentially perpendicular to the capture surface.

In one embodiment wherein the median planes of 2 or more of the divisional unit spacings for pair wise neighbouring divisional units are angled, preferably with an angle between 45 and 135°, more preferably said 2 or more of the divisional unit spacings for pair wise neighbouring divisional units are perpendicular to each other. In this embodiment the median planes may e.g. be essentially perpendicular to the capture surface. Thereby the median planes for the respective divisional unit spacings for pair wise neighbouring divisional units may form a checked pattern when seen from the direction of the capture surface.

In one embodiment where the conduct element is encapsulated in a non-conducting material, the divisional unit spacings for pair wise neighbouring divisional units

may be in the form of voids. In this embodiment the divisional units may e.g. be totally separated and the encapsulating non-conducting material may further comprise one or more voids in communication with the divisional unit spacings for pair wise neighbouring divisional units. This embodiment is particularly useful in situations where the sensor unit is supported or integrated with a support element, as this support element may prevent bending. The sensor unit comprising these features may thus be improved in sensitivity for deforming from one sensor state to another by compression/elongation in a direction essentially parallel to the conduct element. The voids in the non-conducting material thus act as an amplifier for deformations in the thickness direction of the divisional unit spacing for pair wise neighbouring divisional units.

In one embodiment the conduct element consists of randomly ordered divisional units.

As it has been explained above the conduct element may in one embodiment consists of a plurality of divisional units dispersed in a disperse material.

The disperse material should have a specific conductivity which is lower than the specific conductivity of the material for the conduct element. In one embodiment the disperse material is essentially non-conductive.

The disperse material may e.g. selected from the group consisting of or preferably selected from the group consisting of silicon nitride, silicon oxide, metal oxides, polymers, such as photo-sensitive polymers, octafunctional epoxidized novalac e.g. SU-8, benzocyclobutnene e.g. BCB, polyimide, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacrylonitrile, polymethylmetacrylate, polytetrafluoroethylene,

polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, bytyl rubber, styrene butadiene rubber and silicon rubber, more preferably said non-conductive material is a octafunctional epoxidized novalac, more preferably said disperse material being a polymer in particular a octafunctional epoxidized novalac.

The disperse material should preferably be a polymer material. Preferred materials include an epoxy resin, preferably selected from the group consisting of epoxy functional resin having at least two epoxy groups, preferably an octafunctional epoxidized novalac. Particularly preferred materials are described in US 4882245, which is hereby incorporated by reference. The most preferred material is the octafunctional epoxidized novalac which is commercially available from Celanese Resins, Shell Chemical, MicroChem Inc under the trade name SU-8, and from Softec Microsystems under the trade name SM10#0.

The divisional units dispersed in the disperse material may e.g. be of one or more materials selected from the group consisting of amorphous polysilicon (single crystal Si), metal or metal containing composition e.g. gold, AlN, Ag, Cu, Pt and Al, semi-conductors, carbon black, carbon fibres, particulate carbon, carbon nanowires, silicon nanowires.

In one embodiment the divisional units dispersed in the disperse material is of one or more materials selected from the group consisting of metal or metal ion particles such as beads or fibers; carbon black having a specific surface area between 25 and 300 m^2/g, such as Carbon Black # 5500, Tokai Carbon K.K., with a specific surface area of 215 m^2/g or Toka Black #4500, Tokai Carbon K.K., with a specific surface area of 58 m^2/g; carbon fibres, particulate carbon, carbon nanowires and silicon nanowires.

In one embodiment the divisional units dispersed in the disperse material is of carbon nanowires such as nanotubes.

The nanowire is defined as an elongated nanoscale semiconductor which, at any point along its length, has at least one cross-sectional dimension and, in some embodiments, two orthogonal cross-sectional dimensions less than 500 nanometers, preferably less than 200 nanometers, more preferably less than 150 nanometers, still more preferably less than 100 nanometers, even more preferably less than 70, still more preferably less than 50 nanometers, even more preferably less than 20 nanometers, still more preferably less than 10 nanometers, and even less than 5 nanometers. The nanowires have a core and an outer region, the above dimensions relate to those of the core. The cross-section of the elongated semiconductor may have any arbitrary shape, including, but not limited to, circular, square, rectangular, elliptical and tubular. Regular and irregular shapes are included. As used herein, a "nanotube" is a nanowire that has a hollowed-out core, and includes those nanotubes know to those of ordinary skill in the art. A "non-nanotube nanowire" is any nanowire that is not a nanotube. Further information about these useful nanowires can be found in WO 0248701 which is hereby incorporated by reference.

In one embodiment the sensor shaped as described in PA 2002 00125 DK with the difference that the piezoresistor disclosed in PA 2002 00125 DK is replaced with one or more conduct elements as described above. The disclosure concerning shape of sensors of PA 2002 00125 DK is hereby incorporated by reference.

In one embodiment the wires for the sensor is arranged as described in PA 200200283 which is hereby incorporated by reference.

In one embodiment the sensor may be driven by an actuator e.g. comprising a piezoelectric element.

In one embodiment the sensor unit comprises one or more interaction chambers, e.g. as described in WO 0066266. The capture surface(s), or at least one should be exposed to a fluid in at least one interaction chamber.

In one embodiment it is desired that the size of the interaction chamber or chambers individually from each other with a volume of up to about 1 ml, such as up to about 0.1 ml, such as up to about 0.05 ml such as up to about 1 µl, such as up to 0.1 µL.

In one embodiment the sensor unit comprises one or more channels for introducing the sample. The capture surface(s) should be exposed to a fluid in at least one channel. In one embodiment it is desired that the cross dimensions of the channel should be sufficiently small to provide for a laminar flow of a fluid sample through the channel. The channel(s) may e.g. have a cross sectional dimension of up to 250000 μm^2, such as up to 100000 μm^2, such as up to 25000 μm^2, such as up to 2500 μm^2.

In one aspect of the invention the sensor comprising a sensor unit having a capture surface, and comprising at least one conduct element and a pair of wires capable of applying an electrical field over the conduct element, wherein the conduct element is in the form of randomly ordered divisional units dispersed in a disperse material, said divisional units being of an electrically conductive material, said disperse material preferably being non-conductive.

Variations and embodiments of this aspect have been further described above.

In one aspect of the invention the sensor comprises a sensor unit having a capture surface, which sensor unit is capable of being in at least two sensor states and is capable of being deformed from one sensor state to another. The sensor unit comprises at least one conduct element of an electrically conducting material encapsulated in a non-conductive material. The conduct element has a larger conductance in one sensor state than in another sensor state.

The invention also relates to a method of detecting at least one target substance in a fluid sample. The fluid may sample may in principle be any type of flowable material including, liquid, gas, vapour, dust, small beads (e.g. with a particle size less than 100 µm). Preferably the fluid is liquid or gas. The method includes using a sensor as described above, said method comprising the steps of

i. applying the fluid sample to the sensor so that at least one capture surface comes into contact with the sample,
ii. applying a voltage over the sensor so the a voltage is applied over at least one sensor unit with a capture surface in contact with the sample,
iii. measuring an electrical parameter of one or more conduct elements, including at least one conduct element of a sensor unit with a capture surface in contact with the sample,
iv. correlating the result of the measurements to the

detection of the substance.

The electrical parameters may e.g. be conductance and resistance.

The sensor according to the invention may in principle be used as any similar prior art sensor for detecting at least one target substance in a fluid sample. Suitable methods and applications for the sensor according to the invention includes the detection's disclosed in WO 0066266, US 6289717, WO 0133226, and WO 0220832 where the sensor is replaced by the sensor of the invention and where the read out is a direct read out of the change of conductance.

In the following the invention will be further described with reference to the figures and examples.

BRIEF DESCRIPTION OF DRAWINGS

Figure 1 is a schematic illustration of a sensor unit according to the invention in the shape of a cantilever, shown as a sectional side cut along the length axis of the cantilever.

Figure 2 is a schematic illustration of the sensor unit shown in figure 1 seen in the sectional cut A-A.

Figure 3a is a schematic illustration of a conduct element with physically separated divisional units, shown as a sectional side cut.

Figure 3b is a schematic illustration of a conduct element with partly attached divisional units, shown as a sectional side cut.

Figure 3c is a schematic illustration of a conduct element with divisional units dispersed in a disperse material, shown as a sectional side cut.

Figure 4a is a schematic illustration of a bridge shaped sensor unit, shown from above with indication of electrical contact pads.

Figure 4b is a schematic illustration of a disc shaped sensor unit, shown from above with indication of electrical contact pads.

Figure 4c is a schematic illustration of a cantilever shaped sensor unit, shown from above with indication of electrical contact pads.

Figure 5a is a schematic illustration of a section on a sensor unit.

Figure 5b is a schematic illustration of different sizes of divisional units and spacings between neighbouring divisional units.

Figure 6a and 6b are schematic illustrations of a sectional side cut of a sensor unit in section in, respectively, a first and a second sensor state.

Figures 7a and 7b are schematic illustrations of a conduct element with physically separated divisional units, shown as a sectional side cut, for a sensor unit in, respectively, a first and a second sensor state.

Figure 7c is a schematic illustration of a conductance function in relation to the transition from one sensor state to another as illustrated in figures 7a and 7b.

Figures 8a and 8b are schematic illustrations of a conduct element with partly attached divisional units, shown as a sectional side cut, for a sensor unit in, respectively, a first and a second sensor state.

Figure 8c is a schematic illustration of a conductance function in relation to the transition from one sensor state to another as illustrated in figures 8a and 8b.

Figures 9a and 9b are schematic illustrations of a conduct element comprising divisional units dispersed in a disperse material, shown as a sectional side cut, for a sensor unit in, respectively a first and a second sensor state.

Figure 9c is a schematic illustration of a conductance function in relation to the transition from one sensor state to another illustrated in figures 9a and 9b.

Figure 10 is a schematic illustration of a process sequence for fabrication of a cantilever sensor unit for a sensor according to the invention.

DETAILED DESCRIPTION OF THE DRAWINGS

Figure 1 and figure 2 shows a sensor unit 1 shaped as a cantilever with an essentially rectangular outer periphery. In general the shape of the outer periphery of the cantilever is not important. The cantilever may e.g. the dimensions width : height : length of 1-200μm : 0.1-10 μm : 10-400 μm. The main axis along its length axis is illustrated by the cut line A-A'. The sensor unit 1 comprise a first and a second major surfaces 3a, 3b wherein one of the major surfaces 3a constitute a capture surface and comprises a number of binding partners 5. The sensor unit 1 is capable of being mechanically deformed

both by bending and twisting and by extension along the main axis A-A'.

The sensor unit 1, comprises a conduct element 2 encapsulated in a non-conducting, insulating material 4 which prevents short-circuiting of the electrical connections during operation of the sensor in a liquid or moist environment. The thickness of the insulating material 4 is shown exaggerated in figure 1 and 2. The conduct element 2 is divided into at least two not shown divisional units, of an electrically conducting material. The divisional units may be as described above e.g.:
-physically separated from each other with no contact area between neighbouring divisional units, or
-partly connected with a basis common for all the divisional units, or
-the conduct element may comprise divisional units, e.g. randomly ordered, forming a dispersion in a disperse material implying a distribution of sizes of contact areas between divisional units.

Figures 3a, 3b and 3c shows 3 different examples of conduct elements 31, 32 and 33, which can e.g. constitute all or a part of the conduct element 2 as illustrated in figures 1 and 2. These conduct elements will be further described below. Conduct elements 31, 32 and 33 are illustrated comprise rectangular outer periphery including the voids/disperse material between the divisional units. It should be understood that the outer periphery of the conduct elements could in principle have any shape e.g. be horse-shoe shaped.

The cantilever shaped sensor unit 1 is connected to a primary substrate 8 so that the cantilever protrudes and stems from the substrate 8. The substrate 8 is much thicker than the cantilever, so that a deformation

applied onto one of the major surfaces 3a, 3c of the cantilever 1, will primarily act to deform the cantilever and not to deform the primary substrate.

In figure 2 the cantilever shaped sensor unit 1 is seen from above in the sectional cut along the lone A-A'. The conduct element 2 resembles a horse-shoe in shape. The conduct element 2 is encapsulated in a non-conductive material 4. The lanes 2a, of the horse-shoe formed conduct element may e.g. be 5-100 μm in width. The conduct element 2 may be sectioned along the lanes 2a as shown in figure 3a or in part as shown in figure 3b. Two contact pads 7 as seen in figure 1, are not covered by the non-conducting material allowing an electrical connection between the conduct element 2 and a pair of wires 6 of an electrically conducting material. The wires 6 are themselves also fully encapsulated in an insulating material 4.

The conduct element 2 may be sectioned along the lanes 2a, which sectioning is either fully as shown in figure 3a or in part as shown in figure 3b and the binding partners 5 is provided on the insulating layer 4 in the immediate vicinity of spacings between the divisional units. The binding partner thereby being associated to the pair or pairs of divisional units besides the spacing or spacings.

In figure 4c a similar cantilever shaped sensor 43 seen from above and with contact pads 44 are shown. For a bridge shaped sensor unit 42 and a diaphragm shaped sensor unit, also seen from above, the contact pads 44 may be as shown in figure 4a and 4b, respectively.

Now referring to figure 3a which illustrates a conduct element 31 or a section thereof. The conduct element 31

is composed of divisional units 34 of an electrically conductive material. The divisional units are physically separated from each other with voids 34a in between the divisional units. In the example shown in figure 3a the voids are in the form of air, but it should be understood that the voids may be replaced by spacing of non-conducting material or less conducting material than the conduct element, wherein the spacing may be of any fluidic materials such as other gasses or liquids, that can be forced out totally or partly to thereby make contact between the divisional units possible. In principle the voids could also be vacuum, however in this case the not shown insulation around the conduct element should have a balanced stiffness, so that the divisional units can be held apart from each other in one sensor state and be in contact with each other in another sensor state.

The contact areas 34b of the divisional units, i.e. the faces of the divisional units capable of being in contact with each other in at least one sensor state, are totally separated from each other in figure 3a, and consequently the conduction through the conduct element is zero.

Now referring to figure 3b which illustrates a conduct element 32 or a section thereof. The conduct element 32 is composed of divisional units 35 of an electrically conductive material. The divisional units are partly separated from each other with voids 35a in the form of trenches 35a in the conduct material on the cross of the conducting direction. The voids could be as described for the conduct element shown in figure 3a, including in the form of spacings.

The trenches 35a has different depth. The contact areas 35b of the divisional units, i.e. the faces of the

divisional units capable of being in contact with each other in at least one sensor state, are maximal separated from each other in figure 3b. Consequently, the conductance of through the conduct element is lowest possible.

Now referring to figure 3c which illustrates a conduct element 33 or a section thereof. The conduct element 33 is composed of divisional units 37 in the form of particles of an electrically conductive material dispersed in a disperse material 37a. The divisional units are randomly distributed in the disperse material so that at least some of the particles are physically separated from each other with the disperse material 37a in between the divisional units. The disperse material should be sufficiently mouldable so that it is possibly to bring at least some of the separated unit into physically contact by deforming the conduct element.

Figure 5a shows the conduct element 31 of figure 3a encapsulated in a non conductive material. The divisional units 34 are physically separated from each other with voids 52, which include the voids 34a as shown in figure 3a, but also include voids 53 in the insulation material in communication with the voids 34a. The voids 53 in the insulating material e.g. in the form of depressions or trenches into the insulating material 51, provide the insulating material with a weakness in the insulation material so that the force necessary to bring the contact areas 34b of neighbouring divisional units in contact is decreased, which thereby provides an increased sensitivity of the sensor unit. As shown, the voids 53 in the insulating material may have different shape and/or depth.

OPERATION OF THE SENSOR UNIT

Figure 6a is a schematic illustration of a cantilever as disclosed in figures 1 and 2, shown in two different sensor states. The sensor unit 1 is in figure 6a in a sensor state where no interaction between a substance 9 in a sample and the binding partners 5 of the capture layer has taken place. In operation, the sensor unit 1 is subjected to a sample containing a target substance 9 to be detected. In figure 6b the above mentioned interaction has taken place for five binding partners 5 of similar type and a deformation of the sensor unit 1 has resulted due to surface stress caused by the interaction thereby causing the sensor to transit from one sensor state to another. The deformation is shown as a bending, but may also be an elongation/compression or a combination of a bending and an elongation/compression. The deformation may also be a twisting. The deformation depend basically on the shape of the sensor unit and the placement of the capture surface or surfaces.

The transition from one sensor state to another may take place with any suitable choice of types of conduct element 31, 32, 33 shown schematically in figures 3a, 3b, 3c, respectively. The above mentioned transition from one sensor state to another is shown schematically for the type in figure 3a in figures 7a and 7b, for the type in figure 3b in figures 8a and 8b, and for the type in figure 3c in figures 9a and 9b. Common to all three types of conduct elements 31, 32, 33 is the occurrence of a change in contact area for an electrical current flow through the conduct element 2 during the transition. The conductance, or alternatively the resistance, is measured from before the transition until after the transition by

means of the wiring 6 applied with a voltage and suitable means for measuring resistance. In the following description it is chosen to define the functional behaviour of the function in terms of the conductance, given the choice of selecting among the electrical parameters of either conductance or resistance. The change in contact area for the electrical current is correlated to a change in conductance and a function of the conductance with respect to contact area for electrical conduction is thereby obtained. The characteristics of this conductance function are thereafter used to determine, if the target substance is present or not.

In the following, three examples are given for the functional behaviour of the conductance, with reference also to figures 6a and 6b.

In figure 7c one possible conductance function 101a is depicted with relation to the transition illustrated in figures 7a and 7b. The conductance starts out with a zero 101 value before any deformation of the sensor unit 1 has taken place and this zero value 101 thus represents the first state corresponding to figure 7a. In the course of the increasing number of interactions taking place between the binding partners and the substance to the sensor unit 1 gradually deforms and inevitably brings pairs of neighbouring divisional units 104 together due to the deformation and an accompanying contact for electrical conduction between pairs of divisional units 104 is established, see figures 7a and 7b. It is envisaged that after a contact is established between a first pair, a slight increase in the deformation of the sensor unit 1 thereafter brings the second and third pair together to establish contact and thereafter, a current is allowed to run in the now established closed circuit

through the conduct element 2. This final state corresponds to the illustration of the conduct element 2 in figure 7b. The transition from one sensor state to another described above is reflected in figure 7c.

In figure 8c one possible conductance function 111a is depicted with relation to the transition illustrated in figures 8a and 8b. The conductance starts out with a non-zero value 111 before any deformation of the sensor unit 1 has taken place representing the first state corresponding to figure 8a. A non-zero value is due to the conductance through the basis for the divisional units for this particular type of conduct element 2. As interactions are taking place between the binding partners and the substance the sensor unit 1 deforms and brings two neighbouring divisional units together and a first jump 112 in conductance is monitored, see figure 8c. An increase in the deformation of the sensor unit 1 thereafter causes a second pair of divisional units to establish contact and a second jump 113 is monitored for the conductance function 111a, see figure 8c. The establishment of clearly separated jumps in conductance is due to the design of the conduct element 2 and specifically the spacings 118, 119, 120 between neighbouring divisional units. The spacings 118, 119, 120 forms trenches the conduct element. The trenches have different depth, whereby the deepest trench 118, sets the limitation for the conductance. The first jump 112 occurred due to increased contact area between the two neighbouring divisional units on each side of the spacing 118 forming the deepest trench. The second jump 113 occurred due to increased contact area between the two neighbouring divisional units on each side of the next-smallest spacing 119 forming the second deepest trench. The third and final jump 114 occurred due to increased contact area between the two neighbouring divisional

units on each side of the largest spacing 120 forming the third deepest trench. When the third jump 114 has occurred the resulting sensor state corresponds to the illustration of the conduct element 2 in figure 8b. In the above description of the transition from one sensor state to another it is assumed that the binding partners are distributed evenly and that the interaction with the substance ~~10~~ is also occurring evenly. The change in conductance illustrated in figure 8c is characterised as three jumps 112, 113, 114 in conductance corresponding to well separate establishments of contact between the three pairs of divisional units in time. The function may be characterised as a stepwise function 111a with a small equalling of step height.

In figure 9c one possible conductance function 121a is depicted with relation to the transition illustrated in figures 9a and 9b. The conductance starts out with a non-zero value 121 before any deformation of the sensor unit 1 has taken place representing the first state corresponding to figure 9a. A non-zero value 121 is due to the conductance through the randomly occurring paths 123 of conductance enabled by the contact between the dispersed divisional unit in the non-conducting disperse material for this particular type of conduct element 2 as shown in figure 6. As interactions are taking place between the binding partners and the target substance ~~10~~ the sensor unit 1 deforms and the volume of the sensor unit 1 holding the dispersed divisional units are subjected to a compressive stress, see also below. The corresponding variation in conductance with an increasing compression stress is anticipated to be continuous and exponential growing, see figure 9c, due to the formation of more paths 123 for conduction when compressing the material. It is assumed that the volume of the conduct element 2 holding the randomly occurring paths 123 of

conductance between the dispersed divisional unit is solely in the region 122 of the non-conducting disperse material above the neutral axis 124 of the sensor unit 1. In the description of the transition it is assumed that the binding partners are distributed evenly and that the interaction with the target substance ~~10~~ is also occurring evenly. The neutral axis 124 is defined as being contained in the imaginative plane through the sensor unit 1 where compression and tension forces are equal during bending. This assumption implies that the paths of conductance solely occur in the volume where compressive stresses prevail. The change in conductance illustrated in figure 9c is characterised as a continuously growing exponential function 121a.

EXAMPLES

In the following three examples of fabrication of sensor devices, polymers may be used to define the insulating and conducting layers of the sensor devices. A photosensitive polymer octafunctional epoxidized novalac, e.g. SU-8 is used. SU-8 is inherently a good electrical insulator and is furthermore a good diffusion barrier and is chemically inert. Thus, it can be used to protect electrical devices from conducting liquids. The electrical properties of the SU-8 and other polymers and epoxies can be changed by chemically doping the polymer, by ion implantation or by dispersing conducting particles in the polymer. The sensor devices is functionalised after the fabrication.

EXAMPLE 1

FABRICATION OF A CANTILEVER

Figure 10a-h shows a schematic illustration of a process sequence for fabrication of a cantilever sensor unit.

Sensor unit with separated divisional units

First a Si wafer (figure 10a), is coated with an insulating polymer. The polymer is spin coated on the Si surface and the layer will typically have a thickness of 3 µm. The polymer is patterned using standard UV lithography (figure 10b). Next, a layer of Ti/Au is deposited in the thickness 50/2000 Å (figure 10c). The layer is deposited by e-beam evaporation, where the thickness can be controlled within a few Å. Next, an e-beam resist is deposited and an etch mask is defined by e-beam lithography or by nanoimprinting (figure 10d). The Au layer is etched all the way through in KI and the Ti is removed in a short etch in BHF (figure 10e). The resist is removed in acetone and a second layer of insulating polymer is deposited with a thickness of 0.5 µm (figure 10f). The insulating polymer is patterned by UV lithography, whereby the shape of the sensor unit and the contact pad holes are defined (figure 10g). A 50 Å/1000 Å Cr/Au layer for electrical contact is deposited and patterned. Finally, the layered polymer/metal/polymer structure is released from the front side or back side by the wet Si etch TMAH or dry silicon reactive ion etching, resulting in a cantilever structure (figure 10h).

SENSOR UNIT WITH PARTLY CONNECTED DIVISIONAL UNITS

To fabricate a cantilever sensor unit with partly connected divisional units, step 10c- 10e above is modified as follows: First, a resist is spun on the

insulating polymer and patterned by UV lithography. The pattern defines the bottom, connected part of the conduct elements. A 50Å/1000Å Cr/Au layer is deposited and patterned by lift-off technique. Then, an e-beam resist is deposited on the surface and patterned by e-beam lithography. Hereby, the spacing between the divisional units is defined. A 1000 nm thick layer of AU is e-beam deposited and the Au pattern is defined by lift off.

SENSOR UNIT WITH RANDOMLY DISPERSED PARTICLES AS DIVISIONAL UNITS

To fabricate a cantilever sensor unit randomly dispersed particles as divisional units step 10c- 10e above is modified as follows: A polymer with dispersed carbon particles is spin coated on top of the insulating polymer. The polymer has a carbon wt % of approximately 30. The carbon filled polymer is patterned by a lithographic step

CLAIMS:

1. A sensor comprising a sensor unit having a capture surface, which sensor unit is capable of being in at least two sensor states and is capable of being deformed from one sensor state to another, said sensor unit comprising at least one conduct element of an electrically conducting material, which conduct element comprises at least two divisional units, said conduct element having a larger conductance in one sensor state than in another sensor state; said sensor further comprising a pair of wires capable of applying an electrical field over the conduct element, said change in conductance preferably being provided by a change in contact area for electrical conduction between two or more divisional units.

2. A sensor according to claim 1, wherein said sensor unit is capable of being deformed from one sensor state to another due to a surface stress of said sensor unit, said surface stress preferably being less than 10^{-6} N/m, such as less than 10^{-5} N/m, more preferably less than 10^{-4} N/m, more preferably less than 10^{-3} N/m, even more preferably less than 10^{-2} N/m.

3. A sensor according to claim 2, wherein said surface stress is due to a chemical interaction at the capture surface.

4. A sensor according to claim 2, wherein said surface stress is due to a physical interaction at the capture surface.

5. A sensor according to claim 2, wherein said surface stress is due to a temperature change in the capture surface.

6. A sensor according to any one of the preceding

claims, wherein said sensor unit is capable of being deformed from one state to another due to a deformation force of less than 10^{-10} N, preferably less than 10^{-9}-10^{-7} N, more preferably less than 10^{-7}-10^{-5} N, even more preferably less than 10^{-5}-10^{-3} N.

7. A sensor according to claim 6, wherein the sensor unit is essentially sheet-formed with a first and a second major surface, the deformation force being applied against one of the major surfaces, said deformation force preferably being applied against one of the major surfaces in a direction perpendicular +- 45 ° to one of the major surfaces, such as in a direction perpendicular +- 15 ° to one of the major surfaces.

8. A sensor according to claim 6, wherein the sensor unit is essentially sheet-formed with a first and a second major surface, the deformation force being applied in a direction substantially parallel to one or both of the major surfaces of the sensor unit.

9. A sensor according to any one of the preceding claims 1-8, wherein said capture surface is provided by one or more binding partners, such as up to 10 binding partners, such as up to 100 binding partners, such as up to 1000 binding partners, such as up to 10000 binding partners, such as up to 10^{12} binding partners.

10. A sensor according to any one of the preceding claims wherein said capture surface is provided by a capture layer comprising one or more binding partners, such as up to 10 binding partners, such as up to 100 binding partners, such as up to 1000 binding partners, such as up to 10000 binding partners, said capture layer optionally comprising other molecules, such as inert molecules, or molecules that amplify the surface stress.

11. A sensor according to any one of the preceding

claims wherein said capture surface is provided by a capture layer comprising one or more of the materials selected from the group consisting of metals, such as Au, Ag and Pt and polymeric materials, such as polymeric materials selected from the group consisting of thermoplastics such as thermoplastic elastomers including block copolymer such as SEBS, SBS, SIS, TPE-polyether-amide, TPE-polyether-ester, TPE-urethanes, TPE PP/NBR, TPE-PP/EPDM, TPE-vulcanisates and TPE-PP/IIR; rubbers such as butadiene rubber, isoprene rubber, silicon rubber, nitrile rubber, styrene-butadiene rubber and urethane rubber; acrylates; polyolefins such as polyethylene, polypropylene and polybutylene including its isomers; polyesters; polystyrene; polyacrylates; polyethers; and polyurethane.

12. A sensor according to any one of the preceding claims, wherein said capture layer is provided by a capture layer comprising a coating of a material selected from the group consisting of oxides, sulphides and selenides.

13. A sensor according to any one of the preceding claims, wherein the capture surface comprises a plurality of binding partners, said capture surface e.g. being provided essentially by a plurality of binding partners.

14. A sensor according to any one of the preceding claims, wherein the capture surface comprises one or more binding partners in the form of one or more of the binding components selected from the group comprising one or more biomolecules of microbial, viral, fungal, plant, animal or human origin, synthetic molecules resembling them, explosives, alcohols, and drugs, the binding components preferably comprise one or more molecules selected from the group consisting of proteins, glyco proteins, nucleic acids, such as RNA, DNA including cDNA, PNA, LNA, oligonucleotides, peptides, hormones,

antigens, antibodies, lipids, sugars, carbohydrates, and complexes including one or more of these molecules, said biomolecule or molecules preferably being selected from the group consisting of nucleic acids, antibodies, proteins, protein complexes, enzymes, drugs and receptors.

15. A sensor according to any one of the preceding claims, wherein the capture surface comprises one or more binding partners in the form of molecules comprising a functional group selected from the group consisting of -OH, -CHO, -COOH, -SO3H, -CN, -NH2, -SH, -COSH, COOR, halide.

16. A sensor according to any one of the claims wherein the capture surface comprises one or more binding partners which are non-specific.

17. A sensor according to any one of the claims wherein the capture surface comprises one or more binding partners which are specific, said one or more specific binding partners preferably being specific for one or more target components e.g. components including one or more biomolecules of microbial, viral, plant, animal or human origin, synthetic molecules resembling them, explosives, alcohols and/or drugs, more preferably selected from the group consisting of bacterium, virus, fungus, proteins, glyco proteins, nucleic acids, such as RNA, DNA including cDNA, PNA, LNA, oligonucleotides, peptides, hormones, antigens, antibodies, lipids, sugars, carbohydrates, and complexes including one or more of these molecules, said biomolecule or molecules preferably being selected from the group consisting of nucleic acids, antibodies, proteins, protein complexes, enzymes, drugs and receptors.

18. A sensor according to any one of the claims, wherein the conduct element is encapsulated in a non-

conductive material, preferably selected from the group consisting of silicon nitride, silicon oxide, metal oxides, polymers, such as photo-sensitive polymers, octafunctional epoxidized novalac e.g. SU-8, benzocyclobutene, e.g. BCB, polyimide, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacrylonitrile, polymethylmetacrylate, polytetrafluoroethylene, polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, butyl rubber, styrene butadiene rubber and silicon rubber, more preferably said non-conductive material is a octafunctional epoxidized novalac.

19. A sensor according to claim 18, wherein the non-conductive material forms on the conduct element a layer of a thickness of at least 0.1 times the thickness of the conduct element, preferably 0.5 times the thickness of the conduct element, more preferably 1 time the thickness of the conduct element, even more preferably 2 times the thickness of the conduct element.

20. A sensor according to any one of the claims 18 and 19, wherein the non-conductive material forms a layer on the conduct element which conduct element comprises two major surfaces, said layer differing in thickness, preferably so that the layer of non-conductive material onto one of the major surfaces has a first thickness and the layer of non-conductive material onto the other one of the major surfaces has a second thickness.

21. A sensor according to any one of the claims 18-20, wherein the conduct element with the non-conductive material encapsulation comprises two major surfaces, one of said major surfaces comprising an additional layer of a non-conductive or conductive materials selected from the group consisting of silicon nitride, silicon oxide,

metal oxides, polymers, such as photo-sensitive polymers, octafunctional epoxidized novalac e.g. SU-8, benzocyclobutene, e.g. BCB, polyimide, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacrylonitrile, polymethylmetacrylate, polytetrafluoroethylene, polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, butyl rubber, styrene butadiene rubber and silicon rubber, said additional layer may e.g. be doped.

22. A sensor according to any of the preceding claims, wherein the conduct element comprises 3 or more divisional units, such as up to 50 divisional units, such as between 3 and 25 divisional units, such as between 5 and 10 divisional units, said divisional units comprising one contact area for electrical conduction to one or more of the divisional units in one sensor state and no contact area or another contact area for electrical conduction to one or more of the divisional units in another one of the sensor states.

23. A sensor according to claim 22, wherein the capture surface comprises two or more different binding partners, said respective types of binding partners being associated with respective pairs of divisional units so that interaction between a target substance for a first type of binding partner and the first type of binding partner results in an increased contact area for electrical conduction between said pairs of divisional units associated with said first binding partner, and interaction between a target substance for a second type of binding partner and the second type of binding partner results in an increased contact area for electrical conduction between said pairs of divisional units associated with said second binding partner, said contact area for electrical conduction between said pairs of

divisional units associated with said first binding partner is preferably not increased due to interaction between a target substance for a second type of binding partner and the second type of binding partner.

24. A sensor according to claim 23, wherein the binding partner(s) associated with a pair of divisional units is placed relative to the associated pair of divisional units so that a surface stress generated due to interaction with said binding partner(s) results in a force that acts on the associated pair of divisional units to thereby increase the contact area for electrical conduction between said pairs of divisional units, said binding partner(s) preferably being placed on the surface of a non-conductive layer, placed onto one or both of said associated pair of divisional units.

25. A sensor according to claim 24, wherein the first and second binding partner are specific for the same target substance.

26. A sensor according to any one of the above claims, wherein the conductance of the conduct element is a function of the surface stress of the sensor unit.

27. A sensor according to claim 26, wherein said function is a stepwise function, said stepwise function preferably having a number of steps equal to or less than the number of divisional units minus one.

28. A sensor according to claim 26, wherein the height of the steps of said stepwise function is essentially equal to each other.

29. A sensor according to claim 26, wherein the height of the steps of said stepwise function varies, at least two steps having different heights.

30. A sensor according to any one of the preceding claims, wherein the conductance of the conduct element is at least 10^{-7} S in at least one sensor state.

31. A sensor according to any one of the preceding claims, wherein the conductance of the conduct element is less than 10^{-4} S, preferably zero S in at least one sensor state, said sensor unit preferably having two sensor states, and the conductance of the conduct element in the first sensor state is substantially zero S, and the conductance of the conduct element in the second sensor state is different from zero S.

32. A sensor according to any one of the preceding claims, wherein the conductance of the conduct element in one sensor state is at least 2 times, such as at least 3 times, such as at least 5 times the conductance in another sensor state.

33. A sensor according to according to any one of the claims 26-32, wherein said function is a declining function when the surface stress of the sensor unit is decreased.

34. A sensor according to according to any one of the claims 26-33, wherein said function is an increasing function when the surface stress of the sensor unit is decreased.

35. A sensor according to any of the above claims, wherein the conduct element comprises 2-100 divisional units, preferably 2-20 divisional units, more preferably 2-10 divisional units, even more preferably 2-5 divisional units.

36. A sensor according to any of the above claims, wherein one or more of the divisional units of the conduct element have a shape selected from rod-shaped,

slab-shaped, ball-shaped and fibre-shaped.

37. A sensor according to any of the above claims, wherein the contact areas of two neighbouring divisional units which are capable of coming into contact for electrical conduction in one of the sensor states are partly or totally separated from each other to a maximal distance in one sensor state which is designated the max separated sensor state for the two neighbouring divisional units, the space between the contact areas of the two neighbouring divisional units being defined as the divisional unit spacing for the two neighbouring divisional units, the divisional unit spacing for the two neighbouring divisional units having a thickness defined as the distance between the contact areas of the two neighbouring divisional units, the thickness of the divisional unit spacing for the two neighbouring divisional units in the max separated sensor state preferably being up to 1000 nm, such as up to 100 nm, such as up to 10 nm, such as up to 5 nm.

38. A sensor according to claim 37 wherein all of the divisional unit spacings for pair wise neighbouring divisional units have a thickness in their respective max separated sensor states which are up to 1000 nm, such as up to 100 nm, such as up to 10 nm, such as up to 5 nm.

39. A sensor according to any one of the claims 37 and 38 wherein the thickness of one or more of the divisional unit spacings for pair wise neighbouring divisional units varies.

40. A sensor according to any one of the claims 37-39, wherein the divisional unit spacings for pair wise neighbouring divisional units have median planes perpendicular to the thickness direction, 2 or more of the divisional unit spacings for pair wise neighbouring divisional units have median planes which are

substantially parallel to each other.

41. A sensor according to any one of the claims 37-40, wherein the median planes of 2 or more of the divisional unit spacings for pair wise neighbouring divisional units are angled, preferably with an angle between 45 and 135°, more preferably said 2 or more of the divisional unit spacings for pair wise neighbouring divisional units are perpendicular to each other.

42. A sensor according to any one of the claims 37-41, wherein the conduct element is encapsulated in a non-conducting material, the divisional unit spacings for pair wise neighbouring divisional units being voids and said encapsulated non-conducting material comprises one or more voids in communication with the divisional unit spacings for pair wise neighbouring divisional units.

43. A sensor according to any one of the claims 1-23 and 27-39, wherein the conduct element consists of randomly ordered divisional units.

44. A sensor according to any one of the claims 1-22 and 43, wherein the conduct element consists of a plurality of divisional units dispersed in a disperse material, said disperse material preferably being non-conductive.

45. A sensor according to claim 44, wherein the disperse material is a material selected from the group consisting of or preferably selected from the group consisting of silicon nitride, silicon oxide, metal oxides, polymers, such as photo-sensitive polymers, octafunctional epoxidized novalac (e.g. SU-8), benzocyclobutene (e.g. BCB), polyimide, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacrylonitrile, polymethylmetacrylate, polytetrafluoroethylene,

polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, butyl rubber, styrene butadiene rubber and silicon rubber, more preferably said non-conductive material is a octafunctional epoxidized novalac, more preferably said disperse material being a polymer in particular a octafunctional epoxidized novalac.

46. A sensor according to any one of the claims 43-45, wherein the divisional units are of one or more materials selected from the group consisting of amorphous polysilicon (single crystal Si), metal or metal containing composition e.g. gold, AlN, Ag, Cu, Pt and Al, conducting polymers such as, doped octafunctional epoxidized novalac (e.g. doped SU-8), doped benzocyclobutene (e.g. doped BCB) and doped polyimide, semi-conductors, carbon black, carbon fibres, particulate carbon, carbon nanowires and silicon nanowires.

47. A sensor according to any of the claims 1-42, wherein the divisional units are of one or more materials selected from the group consisting of amorphous polysilicon (single crystal Si), metal or metal containing composition e.g. gold, AlN, Ag, Cu, Pt and Al, conducting polymers such as, doped octafunctional epoxidized novalac (e.g. doped SU-8), doped benzocyclobutene (e.g. doped BCB) and doped polyimide, semi-conductors and composite materials with an electrically non-conducting matrix and a conducting filler, wherein the filler preferably is selected from the group consisting of amorphous polysilicon (single crystal Si), metal or metal containing composition e.g. gold, AlN, Ag, Cu, Pt and Al, conducting polymers such as, doped octafunctional epoxidized novalac e.g. doped SU-8, conducting polymers, semi-conductors, carbon black, carbon fibres, particulate carbon, carbon nanowires, silicon nanowires.

48. A sensor according to any one of the preceding claims, wherein all contact areas for electrical conduction between divisional units increase in one transition between a first sensor state and a second sensor state.

49. A sensor according to any one of the claims 1-47, wherein one contact area for electrical conduction between divisional units increases in one transition between a first sensor state and a second sensor state.

50. A sensor according to any one of the preceding claims wherein said sensor unit is shaped as cantilever, a bridge and a diaphragm.

51. A sensor according to any one of the preceding claims, said sensor comprising a primary substrate connected to one or more sensor unit(s), at least one of said wires for applying an electrical field being integrated in said primary substrate, said wire preferably being integrated in said primary substrate by passing through a channel in said primary substrate.

52. A sensor according to claim 54 wherein said primary substrate is of a non-conductive material, said primary substrate comprising one or more of the materials selected from the group consisting of ceramics, silicon, silicon nitride, silicon oxide, metal oxide, glass and polymer, wherein the group of polymers preferably includes epoxy resin e.g. octafunctional epoxidized novalac, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacrylonitrile, polymethylmetacrylate, polytetrafluoroethylene, polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, butyl rubber, styrene butadiene rubber and silicon

rubber.

53. A sensor according to any one of the preceding claims wherein the sensor comprises at least two sensor units, at least one of said sensor units being a reference unit, said reference unit preferably comprising a capture surface, which has a surface chemistry different from the sensor unit for which the reference unit acts as reference, preferably said capture surface on said reference sensor unit comprises one or more binding partners, wherein said one or more binding partners on the capture surface of said reference unit or its concentration are different from the binding partners or the concentration thereof on the capture surface of the sensor unit for which the reference unit acts as reference.

54. A sensor according to any one of the preceding claims, wherein discrimination between the sensor states can be performed by a measurement of an electrical parameter for a circuit comprising the pair of wires and the conduct element.

55. A sensor according to any one of the preceding claims, wherein a conduct element of a sensor unit is a part of a Wheatstone bridge.

56. A sensor according to any one of the preceding claims, said sensor comprises one or more interaction chambers, the capture surface(s) being exposed to a fluid in at least one interaction chamber, preferably individually from each other with a volume of up to about 1 ml, such as up to about 0.1 ml, such as up to about 0.05 ml such as up to about 1 µl.

57. A sensor according to any one of the preceding claims wherein said sensor unit comprises one or more channels, the capture surface(s) being exposed to a fluid

in at least one channel, the channels having an average cross sectional dimension of up to 250000 μm^2, such as up to 100000 μm^2, such as up to 25000 μm^2, such as up to 2500 μm^2, where the average cross sectional dimension of a channel is defined as the diameter of a corresponding channel with circular cross section, where the cross sectional area is equal to the cross sectional area of the channel.

58. A sensor comprising a sensor unit having a capture surface, and comprising at least one conduct element and a pair of wires capable of applying an electrical field over the conduct element, said conduct element being in the form of randomly ordered divisional units dispersed in a disperse material, said divisional units being of an electrically conductive material, said disperse material preferably being non-conductive.

59. A sensor according to claim 58, wherein said sensor unit is capable of being in at least two sensor states and is capable of being deformed from one sensor state to another, said conduct element having a larger conductance in one sensor state than in another sensor state, said change in conductance preferably being provided by a change in contact area for electrical conduction between the divisional units.

60. A sensor according to any one of the claims 58-59, wherein said conduct element comprises a plurality of divisional units.

60. A sensor according to any one of the claims 58-59, wherein the disperse material is a material selected from the group consisting of or preferably selected from the group consisting of silicon nitride, silicon oxide, metal oxides, polymers, such as photo-sensitive polymers, octafunctional epoxidized novalac (e.g. SU-8),

benzocyclobutene (e.g. BCB), polyimide, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacrylonitrile, polymethylmetacrylate, polytetrafluoroethylene, polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, butyl rubber, styrene butadiene rubber and silicon rubber, more preferably said non-conductive material is a octafunctional epoxidized novalac, more preferably said disperse material being a polymer in particular a octafunctional epoxidized novalac.

61. A sensor according to any of the claims 58-60, wherein the divisional units are of one or more materials selected from the group consisting of amorphous polysilicon (single crystal Si), metal or metal containing composition e.g. gold, AlN, Ag, Cu, Pt and Al, conducting polymers such as doped octafunctional epoxidized novalac (e.g. doped SU-8), doped benzocyclobutene (e.g. doped BCB) and doped polyimide, semi-conductors, carbon black, carbon fibres, particulate carbon, carbon nanowires and silicon nanowires.

62. A sensor according to any of the claims 58-61, wherein said sensor unit is capable of being deformed from one sensor state to another due to a surface stress of said sensor unit, said surface stress preferably being less than 10^{-4} N/m, such as less than 10^{-5} N/m, more preferably less than 10^{-4} N/m, more preferably more than 10^{-3} N/m even more preferably less than 10^{-2} N/m.

63. A sensor according to any of the claims 58-62, wherein said sensor unit is capable of being deformed from one state to another due to a deformation force of less than 10^{-10} N, preferably less than 10^{-9}-10^{-7} N, more preferably less than 10^{-7}-10^{-5} N, even more preferably less than 10^{-5}-10^{-3} N.

64. A sensor according to any of the claims 58-63, wherein said capture surface is provided by one or more binding partners, such as up to 10 binding partners, such as up to 100 binding partners, such as up to 1000 binding partners, such as up to 10000 binding partners.

65. A sensor according to any one of the preceding claims 58-64, wherein said capture surface is provided by a capture layer comprising one or more binding partners, such as up to 10 binding partners, such as up to 100 binding partners, such as up to 1000 binding partners, such as up to 10000 binding partners, said capture layer optionally comprising other molecules, such as inert molecules, or molecules that amplify the surface stress.

66. A sensor according to any one of the preceding claims 58-65, wherein the capture surface comprises one or more binding partners in the form of one or more of the binding components selected from the group of group biomolecules of microbial, fungal, plant, animal or human origin or synthetic molecules resembling them, explosives, alcohols and drugs, preferably selected from the group consisting of proteins, glyco proteins, nucleic acids, such as RNA, DNA including cDNA, PNA, LNA, oligonucleotides, peptides, hormones, antigens, antibodies, lipids, sugars, carbohydrates, and complexes including one or more of these molecules, said biomolecule or molecules preferably being selected from the group consisting of nucleic acids, antibodies, proteins, protein complexes, explosives, alcohols and drugs.

67. A sensor according to any one of the preceding claims 58-66, wherein the capture surface comprises one or more binding partners in the form of molecules comprising a functional group selected from the group consisting of -OH, -CHO, -COOH, -SO3H, -CN, -NH2, -SH, -

COSH, COOR, halide.

68. A sensor according to any one of the claims 58-68, wherein the capture surface comprises one or more binding partners which are specific, said one or more specific binding partners preferably being specific for one or more target components selected from the group of components comprising one or more biomolecules of microbial, plant, animal or human origin or synthetic molecules resembling them, explosives, alcohols and drugs, preferably selected from the group consisting of bacterium, virus, fungus, proteins, glyco proteins, nucleic acids, such as RNA, DNA including cDNA, PNA, LNA, oligonucleotides, peptides, hormones, antigens, antibodies, lipids, sugars, carbohydrates, and complexes including one or more of these molecules, said biomolecule or molecules preferably being selected from the group consisting of nucleic acids, antibodies, proteins, protein complexes, explosives, alcohols and drugs.

69. A sensor according to any one of the claims 58-68, wherein the conduct element is encapsulated in a non-conductive material, preferably selected from the group consisting of silicon nitride, silicon oxide, metal oxides, polymers, such as photo-sensitive polymers, octafunctional epoxidized novalac (e.g. SU-8), benzocyclobutene (e.g. BCB), polyimide, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacrylonitrile, polymethylmetacrylate, polytetrafluoroethylene, polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, butyl rubber, styrene butadiene rubber and silicon rubber, more preferably said non-conductive material is a octafunctional epoxidized novalac.

70. A sensor according to claim 69, wherein the conduct element with the non-conductive material encapsulation comprises two major surfaces, one of said major surfaces comprising an additional layer of a non-conductive or conductive material selected from the group consisting of silicon nitride, silicon oxide, metal oxides, polymers, such as photo-sensitive polymers, octafunctional epoxidized novalac (e.g. SU-8), benzocyclobutene (e.g. BCB), polyimide, polystyrene, polyethylene, polyvinylacetate, polyvinylcloride, polyvinylpyrrolidone, polyacrylonitrile, polymethylmetacrylate, polytetrafluoroethylene, polycarbonate, poly-4-methylpentylene, polyester, polypropylene, cellulose, nitrocellulose, starch, polysaccarides, natural rubber, butyl rubber, styrene butadiene rubber and silicon rubber, said additional layer may e.g. be doped.

71. A sensor according to any of the preceding claims 58-70, wherein one or more of the divisional units of the conduct element have a shape selected from rod-shaped, slab-shaped, ball-shaped and fibre-shaped.

72. A sensor according to any one of the claims 58-71, wherein the divisional units of the conduct element are randomly ordered.

73. A sensor according to any one of the claims 58-71, wherein the divisional units of the conduct element are ordered, the divisional units preferably being ordered with respect to directions e.g. fiber directions, and/or concentration.

74. A method of detecting at least one target substance in a fluid sample using a sensor as defined in any one of the preceding claims, said method comprising the steps of

i. applying the fluid sample to the sensor so that at least one capture surface comes into contact with the sample,

ii. applying a voltage over the sensor so the a voltage is applied over at least one sensor unit with a capture surface in contact with the sample,

iii. measuring an electrical parameter of one or more conduct elements, including at least one conduct element of a sensor unit with a capture surface in contact with the sample,

iv. correlating the result of the measurements to the detection of the substance,

said electrical parameter preferably being selected from the group consisting of conductance and resistance.

75. A method according to claim 74, wherein the capture surface in contact with the sample comprises one or more binding partners which are specific for one or more target substances.

76. A method according to any one of the claims 74 and 75, wherein said capture surface in contact with the sample is exposed in a channel, said sample having a laminar flow through said channel.

77. A method according to any one of the claims 74 - 76, wherein the temperature of said fluid is in the interval of 0-100 °C, preferably of 10-90 °C, more preferably of 20-80 °C, even more preferably of 20-50 °C.

1/9

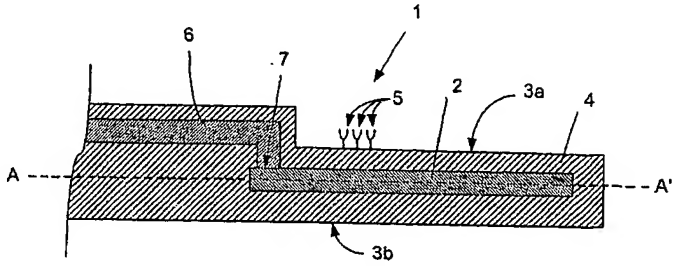

Figure 1

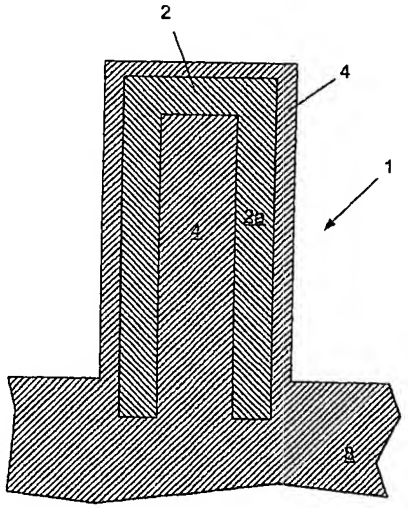

Figure 2

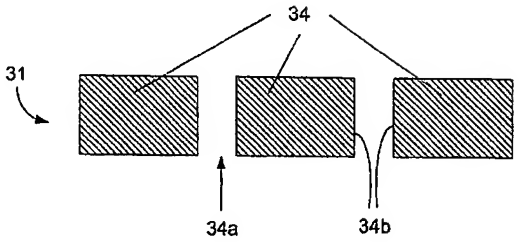

Figure 3a

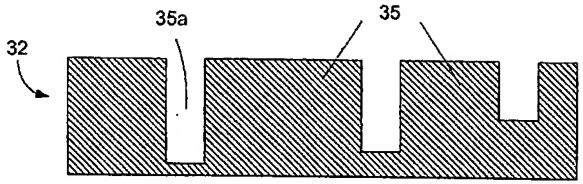

Figure 3b

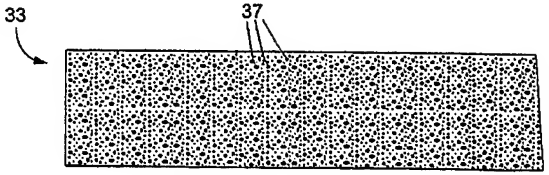

Figure 3c

Figure 4a

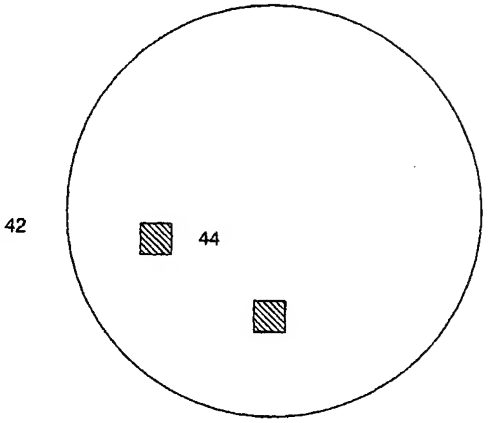

Figure 4b

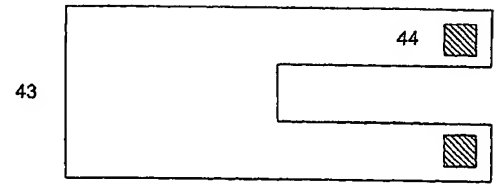

Figure 4c

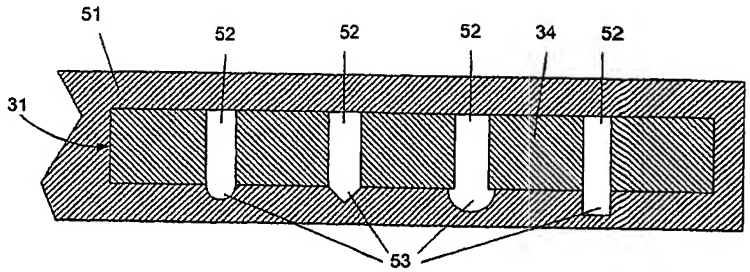

Figure 5a

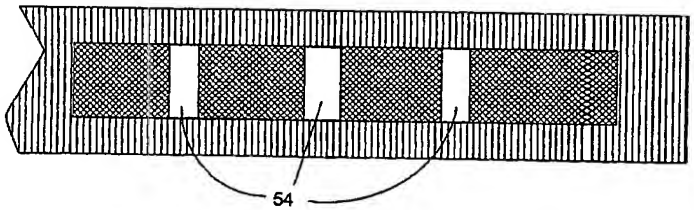

Figure 5b

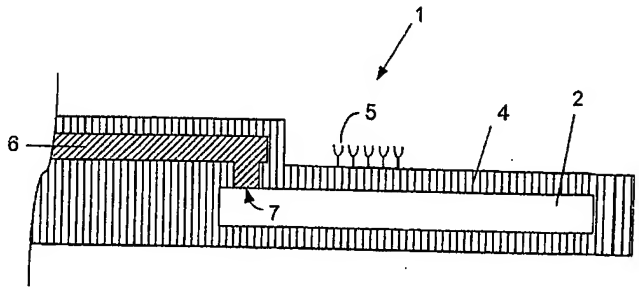

Figure 6a

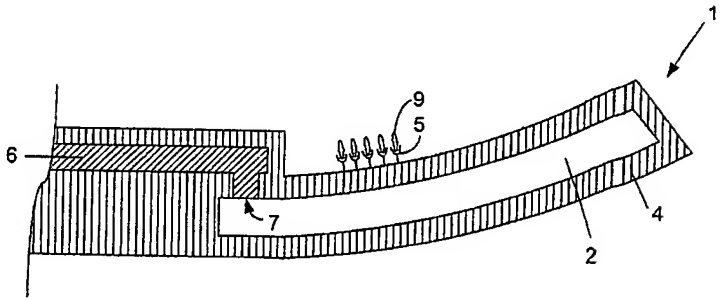

Figure 6b

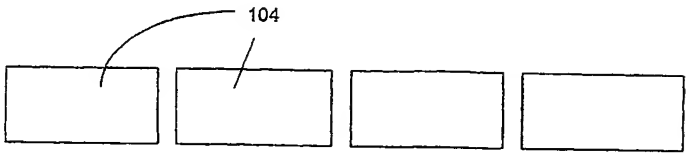

Figure 7a

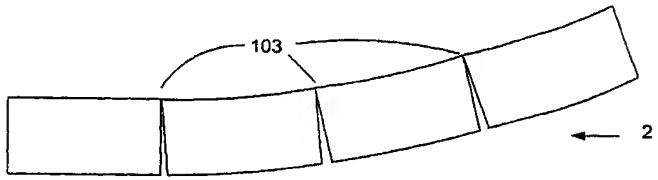

Figure 7b

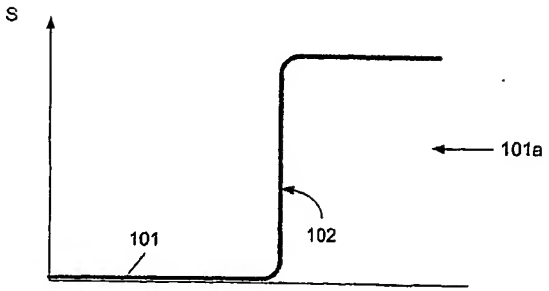

Figure 7c

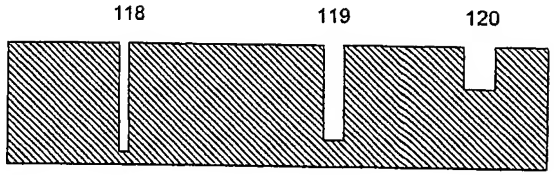

Figure 8a

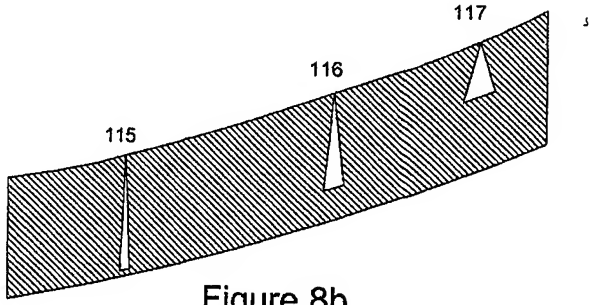

Figure 8b

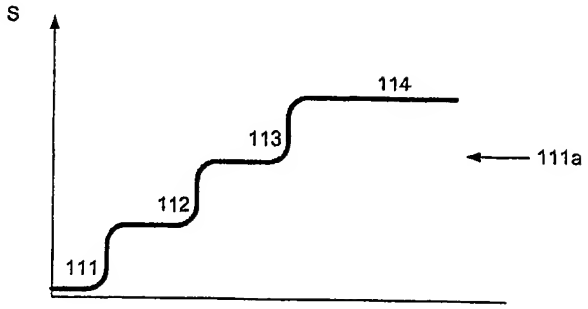

Figure 8c

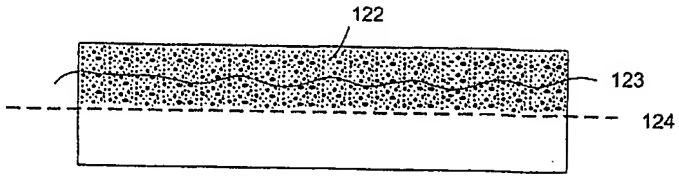

Figure 9a

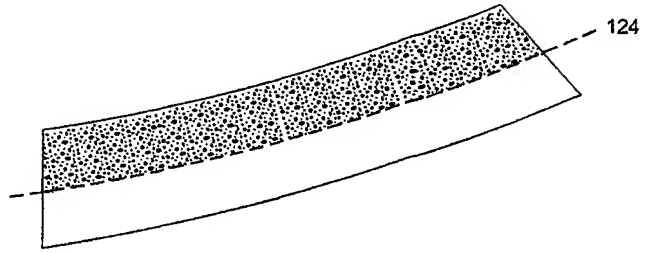

Figure 9b

Figure 9c

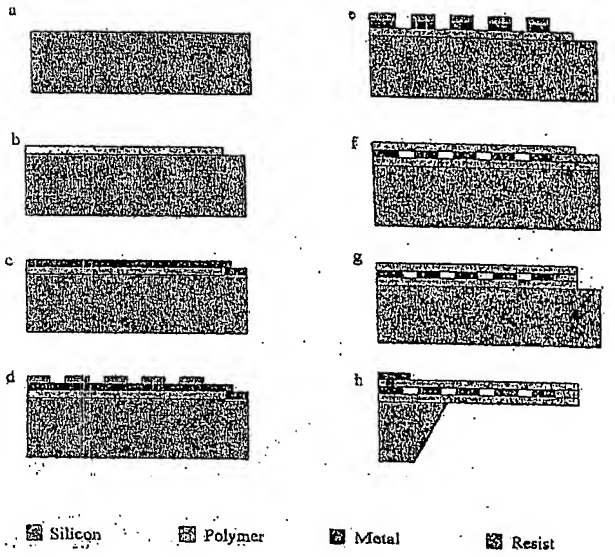

Figure 10

INTERNATIONAL SEARCH REPORT

PCT/EP2005/050785

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N27/12 C12Q1/68 G01N33/543

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, INSPEC, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 256 574 A (NEUBURGER G G ET AL) 26 October 1993 (1993-10-26) column 5, line 3 - column 8, line 55; figures 1-6 ——— -/--	1,4,18, 26, 30-34, 36-43, 54,56, 58-61, 69,70, 72-74,77

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 June 2005	01/07/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Johnson, K

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INTERNATIONAL SEARCH REPORT

PCT/EP2005/050785

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ZEE F ET AL: "Micromachined polymer-based chemical gas sensor array" SENSORS AND ACTUATORS B, vol. 72, no. 2, 25 January 2001 (2001-01-25), pages 120-128, XP004228222 ISSN: 0925-4005 the whole document ———	1-6,18, 26, 43-49, 58-63, 69,72, 74,77
X Y A	EP 1 384 612 A (MATSUSHITA ELECTRIC WORKS) 28 January 2004 (2004-01-28) paragraph '0022! - paragraph '0032! paragraph '0036! - paragraph '0030! paragraph '0049! figures 1-7,11-14 ———	1,2,4, 6-8,12, 18-20, 26,35, 36, 38-42, 47,50, 51,55,56 3,5, 9-11, 13-17, 21, 30-34, 53,54, 57,70-77 22-25, 27-29, 37,46, 58,61-63
Y	THAYSEN J ET AL: "Cantilever-based bio-chemical sensor integrated in a microliquid handling system" PROCEEDINGS OF THE IEEE 14TH. ANNUAL INTERNATIONAL CONFERENCE ON MICROELECTRO MECHANICAL SYSTEMS. MEMS 2001, vol. CONF. 14, 21 January 2001 (2001-01-21), pages 401-404, XP010534633 CATALOG NO 01CH37090 ISBN: 0-7803-5998-4	3,5, 9-11, 13-17, 21, 30-34, 53,54, 57,70-77
A	the whole document ——— -/—	1,2,4, 6-8,12, 18-20, 50-52, 55,56, 61-66, 68,69

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INTERNATIONAL SEARCH REPORT

PCT/EP2005/050785

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TIPPLE C A ET AL: "Nanostructured microcantilevers with functionalized cyclodextrin receptor phases: self-assembled monolayers and vapor-deposited films." ANALYTICAL CHEMISTRY, vol. 74, no. 13, 1 July 2002 (2002-07-01), pages 3118-3126, XP002332633 ISSN: 0003-2700 the whole document	1-11, 14-17, 22,35, 43,46, 47,50, 58, 61-68, 71,72
A	HEADRICK J J ET AL: "Enhancing chemi-mechanical transduction in microcantilever chemical sensing by surface modification" ULTRAMICROSCOPY, vol. 97, no. 1-4, October 2003 (2003-10), pages 417-424, XP002332634 ISSN: 0304-3991 the whole document	1-11, 14-17, 22,35,56
A	WO 02/20832 A (ATONOMICS APS) 14 March 2002 (2002-03-14) cited in the application page 16, line 13 - page 17, line 24 figures 1-4,8; example 1	1-3, 6-11, 13-17, 50, 53-57, 74-77
P,A	KARHADE O G ET AL: "Novel cantilever for biosensing applications" PROCEEDINGS 2004 IEEE INTERNATIONAL SYMPOSIUM ON SEMICONDUCTOR MANUFACTURING CONFERENCE AND WORKSHOP, 2004, pages 409-412, XP002332635 ISSN 1078-8743 the whole document	1-3, 6-10, 13-17, 22-26, 35,50, 74,75

Form PCT/ISA/210 (continuation of second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

PCT/EP2005/050785

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 52
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2004)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 52

Claim 52 refers back to claim 54, so it was not possible to determine the scope of the claim, whereby a meaningful for this subject matter was rendered impossible.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

PCT/EP2005/050785

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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			JP 7018995 Y2		01-05-1995
EP 1384612	A	28-01-2004	JP 2004053424 A		19-02-2004
			CA 2430451 A1		19-01-2004
			CN 1469100 A		21-01-2004
			EP 1384612 A2		28-01-2004
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			WO 0220832 A1		14-03-2002
			US 2003054355 A1		20-03-2003

WIPO 66 pages